

Elusive Features in the Epidemiology of the Common Cold*

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THE common cold is of such frequent occurrence that our opportunities for observing it would seem to be unlimited; yet we have accumulated exceedingly little exact knowledge and less understanding of its epidemiology. We know, in a general way, that it is of world-wide and common occurrence; but we have very scant records of its actual prevalence and distribution in the different elements of any population, still less of its relative prevalence in different parts of the world and in different periods of time.

As to etiology, it is generally believed that the malady is an infection, directly transmissible from person to person, and that certain special circumstances, such as chilling and fatigue, are contributory factors of some importance. These beliefs, however, are based largely upon impressions or so-called common knowledge; they are held somewhat tentatively; and are rather vaguely defined with respect to the nature of the infection—whether it be specific or heterogeneous, primary or secondary—and in the relative importance attached to supposed contributory causes.

In explanation of this backward state of knowledge, there are several features of the common cold which tend to make the collection and interpretation of significant epidemiological data unusually difficult. In the first place, the disease is of such trivial character that, until recent years, it has attracted little serious study except from the angle of bacteriology. Also, because of this triviality, exact records of its prevalence, distribution and clinical course are not obtainable except by elaborate arrangements for special observation of selected groups. Again, the high prevalence of the disease, together with the fact that it causes such slight disability, makes it exceedingly difficult to obtain reliable accounts of the contact relations between cases and even more difficult to interpret such records after they have been collected.

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Then too, the fact that colds usually recur in the same person at intervals of a few months necessitates keeping the same individuals under continuous observation for rather long periods; and moreover, whatever interpretation be placed upon this tendency to recurrence, it implies complexities of epidemiology. However, the most baffling features of the disease are (1) that it lacks sharp clinical definition, and (2) that experimental research has yielded only indecisive results.

Referring first to bacteriological and other experimental investigations, they have been so extensive and varied that many different shadings of interpretation may be given to the findings. It is, however, a reasonably fair summary to say that the results to date leave it in doubt whether the pathological reaction which we call a cold is caused by (1) a specific infection, the same in all cases; (2) infection by any one of various organisms; or (3) some non-infectious process which opens the way for bacterial invasion as a secondary phenomenon. If any more definite general result may be claimed, it is, perhaps, that the trend of recent work has been to strengthen the evidence in favor of infection as the primary process; to indicate that none of the easily cultivated organisms commonly found in the respiratory passages bears a specific relation to the disease; and to point toward a filter-passing organism or group of organisms as the primary and essential cause. These, however, are only suggestive indications, not established conclusions.

The lack of positive aid from the bacteriological laboratory constitutes by itself a sufficiently serious difficulty in the epidemiological study of any supposedly infectious disease; but in the problem of the common cold this deficiency is associated with a lack of clinical definition. The fundamental importance of this is indicated by recalling the general process whereby proof of specific etiology is established.

In the usual order of procedure, the first stage in such proof is recognition of a distinctive clinical-pathological process which serves to identify individual cases with each other and to differentiate them from other diseases. It is the distinctiveness of this reaction which establishes the presumption that the cases manifesting it are due to a common cause which is different from that operative in cases where this clinical reaction is not found; and this presumption of specific (not necessarily infectious) causation is of fundamental importance to further investigation, forming a definite foundation upon which to assemble facts pertaining to the nature of the cause. Moreover, the character of the clinical reaction frequently suggests, by analogy with other diseases, that it either is or is not due to a specific microorganism.

In seeking to test the hypothesis of a specific cause and to learn

something of its nature and the mechanism of its action, we proceed by either or both of two methods: (1) by observation and analysis of special circumstances associated with the natural occurrence of the disease; or (2) by experimental methods, including in this category bacteriological and immunological procedures.

These several stages of proof may proceed coincidentally, or their order may be reversed, so that clinical differentiation may be derived originally from bacteriological observation, as in the distinction between typhoid and paratyphoid fever. But regardless of the sequence, the significance of both epidemiological and experimental evidence, as indicating a specific etiology for the disease in question, depends upon the distinctiveness of the pathological process which constitutes the disease. Obviously it is essential to the proof of specific etiology that the effect as well as the cause be specific.

As regards the common cold, what seems to be the most fundamental difficulty is that we have been unable to identify a clinical-pathological process which is sufficiently distinctive to be confidently accepted as specific. This affects both experimental and epidemiological studies. For example, various observers have succeeded in reproducing, under experimental conditions, reactions which more or less resembled the common cold or influenza, but the experiments have been indecisive because of uncertainty as to whether the experimental disease actually was identical with that occurring naturally in man. For epidemiological investigation a primary requirement is to mark off for study a clinical unit so distinctive as to justify the presumption that it coincides with an etiological unit.

In attempting to locate such a unit, we may begin by excluding from consideration diseases such as measles and the pollen fevers which exhibit symptoms more or less resembling those of the common cold but with other characteristics which readily differentiate them. This leaves in the field a rather large family of what we may call the minor respiratory diseases, all characterized by acute catarrhal inflammation of some portion of the respiratory tract, and a constitutional reaction of moderate severity, manifested by such symptoms as general malaise, headache, aching in the body and limbs, and perhaps fever. In addition to what usually would be called "colds," this family includes cases which, by present usage, are variously designated as influenza, grippe, acute bronchitis, tracheitis, laryngitis, and pharyngitis, respectively, or by some combinations or equivalents of these terms. Granting that these designations correspond to clinical pictures which actually are in some degree different, the question is whether this or any other classification divides the family into groups

of cases which are clinically so distinct as to justify the presumption that the cases within each group are due to one common cause, which is different from the cause of each other group.

Townsend and Sydenstricker¹ have investigated this question by statistical analysis of the clinical records of all the cases of minor respiratory disorders reported during two years in a large group of families, the records being furnished by observers, most of whom were physicians. Assembling the reported cases into four main diagnostic groups, viz.: colds, bronchitis, sore throat, and influenza, they found that these groups differed from each other only in the relative frequency and prominence of symptoms which were more or less common to all, so that the groups overlapped. Moreover, they found that in reporting cases the observers frequently used combinations of the four principal diagnoses, so that altogether more than a dozen diagnostic classes were represented. Interposing the various combinations between the main groups the result is a graded series of variation in clinical types, so that no group differs from its nearest neighbor sufficiently to justify a strong presumption of specifically different causation.

In a smaller but somewhat more intensive study which is now in progress in Baltimore we have observed all the cases of minor respiratory disorders occurring in a group of families in the course of a year. Within the whole series the range of variation in symptoms noted is very wide, extending from acutely febrile cases, conforming to the classical descriptions of epidemic influenza, to simple coryza or tracheitis, with little or no constitutional disturbance. If these extreme types were taken by themselves, they would seem to differ widely enough to justify the inference that they were due to quite different causes; but when the whole series is classified we find, as did Townsend and Sydenstricker, that the extremes are connected by a gradation of intermediate types, so that one does not know where to draw lines of demarcation.

The conclusion drawn from these two studies, namely, that the different clinical types of minor respiratory disorders merge into each other by graded variations, is not at all inconsistent with the fact that separate types are generally recognized in medical literature, for careful reading of the type-descriptions as given by representative writers shows that where lines of differentiation are drawn they are either arbitrary or quite indefinite.

I think then, that if we take into account only *clinical* evidence, it is an open question whether the whole family of these minor respiratory diseases should be considered as varying manifestations of a

single specific cause or as including an indefinite number of separate etiological groups. It is not necessary here to present any argument on either side of the question, or to discuss the prospect that more definitive clinical evidence may be discovered. The point is simply that the clinical evidence now available, taken by itself, does not justify any strong presumption either that the whole family is, or that it is not, a single etiological unit.*

Since neither clinical nor bacteriological observation has enabled us to mark off a definite group of cases which we may assume coincides with an etiological unit, we are in a dilemma with respect to epidemiological studies. If we begin by setting up a restricted clinical definition of the common cold, and confine epidemiological observations to cases coming within this definition, we may be making the same mistake that our forefathers made when they failed to identify membranous croup with other forms of diphtheria, and therefore run the risk of missing important epidemiological associations. On the other hand, if we include the whole family of minor respiratory diseases in one category, we may be obscuring, in the composite, distinctive epidemiological characteristics of its separate components, as would be the case if all the acute exanthemata were thrown into one undifferentiated group, so that facts concerning smallpox were confused with those pertaining to measles and scarlet fever.

The only way out of the difficulty seems to be to include the whole group of minor respiratory diseases in epidemiological studies, but with such detailed clinical and bacteriological records of individual cases as will permit any desired clinical groupings; then to ascertain whether any tentative groupings on a clinical or bacteriological basis correspond to significant epidemiological differences. This procedure has the merit that it involves no assumption as to the unity or diversity of causation for the group as a whole and that it affords the possibility of testing the significance of indistinct clinical differences by matching them against corresponding differences in epidemiological characteristics. However, the method is extremely laborious to carry out, even on a small scale, and obviously small scale studies do not suffice. Comparisons with respect to such features as rate and extent of geographic distribution require observations of the broadest scope.

The principle of seeking by epidemiological characteristics to supplement indistinct clinical differentiation of diseases is, of course, not new. It has been applied for many years in the study of epidemic

* It may be added that this is the usual view, for while many students of the subject, perhaps most of them, consider epidemic influenza a specific disease, distinct from endemic grippé and severe colds, they usually admit, more or less explicitly, that the differentiation is based partly upon epidemiological considerations. It may also be added that for the present bacteriological examination affords no significant basis for differentiation.

influenza, and less extensively in studies of the common cold. For instance, Townsend and Sydenstricker, in the study previously referred to, present statistical analyses of the seasonal and age distribution of cases classified clinically as colds, bronchitis, sore throat, and influenza, respectively, which show that as regards these epidemiological features the several groups differ from each other. To cite only one example, the age distribution of influenza differs from that of colds in their series; but granting that the differences are significant in a statistical sense, the question arises whether they are sufficient to indicate different specific causes.

A possible interpretation is that the age of the individual affected may be a factor in influencing the type of reaction to the same specific cause, as is true in diphtheria, where we find quite different age distributions for the laryngeal and pharyngeal forms of this disease. Likewise, such epidemiological differences as Jordan and others¹ have demonstrated between pandemic and inter-pandemic influenza present similar difficulties of interpretation; and it may be said generally of studies made upon this principle that the difficulties encountered in interpreting their data are even greater than those of collecting them.

CONCLUSION

In conclusion, it appears that the central problem involved in the epidemiology of the common cold is that of its relation to epidemic influenza and other members of the general family of minor respiratory diseases. Two of the approaches to this problem are at present being vigorously attacked by bacteriological and epidemiological studies, respectively; but the more direct approach, by way of clinical and pathological research, has received far less attention.

Considering that the problem is primarily one of identifying a pathological process, and that such identification appears to be fundamental to either bacteriological or epidemiological proof, the most urgent present need in the investigation of the common cold seems to be for more intensive clinical study of the whole group in which it falls.

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